REMARKS

Claims 51-59 were pending in the application. In the instant Amendment, claims 51-53 and 56-57 have been amended to more clearly describe the invention. Upon entry of the above-made amendment, claims 51-59 will be pending.

Claim 51 has been amended to recite that the determined interpolated response profile comprising *measurements of a second plurality of cellular constituents comprising at least a portion of said first plurality, each said measurement being extracted from an interpolated response curve of said measurement as a function of level of said disease state* (emphasis added). Claim 51 has also been amended to recite that said interpolated response curve is obtained by a method comprising (i) providing response profiles of one or more cells of one or more analogous subjects for said disease state, wherein *each* of said response profiles comprises measurements of said second plurality of cellular constituents in one or more cells of *one of* said one or more analogous subjects at *one of* a plurality of levels of said disease state, and (ii) interpolating *measurements of each said cellular constituent in said response profiles over said plurality of levels of said disease state to generate an interpolated response curve* so that an interpolated response profile *comprising measurements of said portion of said first plurality of cellular constituents at a same level of said disease state may be extracted over a range of levels of said disease state* (emphasis added). Claim 51 has also been amended to recite in step (2) determining statistical significance of said *similarity between said interpolated response profile and said diagnostic profile* (emphasis added). Claim 51 has also been amended to replace the term "measured amounts" with the term "measurements." Support of the amendment is found in the specification at page 27, line 30, through page 28, line 2; at page 28, line 17, through page 29, line 26; at page 32, line 32, through page 33, line 2; and at page 17, lines 8-12. Claim 51 has further been amended to make the language clearer. Dependent claims 52-53 and 56-57 have also been amended accordingly.

No new matter has been added by these amendments. Entry of the foregoing amendments and consideration of the following remarks are respectfully requested.

THE STATUS OF THE PRIORITY APPLICATION

The Examiner has required that the status of the nonprovisional parent application be included in the priority statements. Applicants have amended the specification to include such status.

THE TITLE OF THE APPLICATION

The Examiner contends that the title of the application is not descriptive and requires that Applicants provide a new title. Applicants has amended the title as required by the Examiner.

THE OBJECTION TO THE ABSTRACT SHOULD BE WITHDRAWN

The abstract of the disclosure is objected to for exceeding 150 words. Applicants have amended the abstract such that it contains less than 150 words. The objection to the abstraction is therefore obviated and should be withdrawn.

THE REJECTION UNDER 35 U.S.C. § 112, SECOND PARAGRAPH, SHOULD BE WITHDRAWN

Claims 51-59 are rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The Examiner contends that the metes and bounds of interpolation practice are vague. Applicants have amended claim 51 to recite that the determined interpolated response profile comprises *measurements of a second plurality of cellular constituents comprising at least a portion of said first plurality, each said measurement being extracted from an interpolated response curve of said measurement as a function of level of said disease state*, and that said interpolated response curve is obtained by a method comprising (i) providing response profiles of one or more cells of one or more analogous subjects for said disease state, wherein *each* of said response profiles comprises measurements of said second plurality of cellular constituents in one or more cells of *one of* said one or more analogous subjects at *one of* a plurality of levels of said disease state, and (ii) interpolating *measurements of each said cellular constituent in said response profiles over said plurality of levels of said disease state to generate an interpolated response curve* so that an interpolated response profile *comprising measurements of said portion of said first plurality of cellular constituents at a same level of said disease state may be extracted over a*

range of levels of said disease state (emphasis added). The rejection is therefore obviated and should be withdrawn.

THE REJECTIONS UNDER 35 U.S.C. § 102
SHOULD BE WITHDRAWN

Claims 1, 9-12, 15-18, 35, 36, 43 and 45 are rejected under 35 U.S.C. § 102(b) and (e)(2) as being anticipated by Swift et al., U.S. Patent No. 5,464,742 ("Swift"), or, in the alternative, under 35 U.S.C. § 102(e)(2) by Anderson et al., U.S. Patent No. 6,267,722 ("Anderson"). Applicants respectfully disagree with the Examiner for the reasons presented below.

A claim is anticipated under 35 U.S.C. § 102 only if each and every element and limitation as set forth in the claim is found, either expressly described or inherently present, in a single prior art reference. *Glaxo, Inc. v. Novopharm Ltd.*, 52. F.3d 1043, 1047 (Fed. Cir. 1995). There must be *no differences* between the claimed invention and the reference disclosure as viewed by a person of ordinary skill in the field of the invention. *Scripps Clinic & Research Fdn. v. Genentech, Inc.* 927 F. 2d. 1565, 1576 (Fed. Cir. 1991). Anticipation requires that all aspects of the claimed invention were already described in a *single* reference. *Scripps Clinic & Research Fdn. v. Genentech, Inc.* 927 F. 2d. 1565, 1576 (Fed. Cir. 1991).

The presently claimed invention provides a method for diagnosing a level of a disease state of a subject based on a diagnostic profile comprising measurements of a first plurality of cellular constituents in one or more cells of the subject. The claimed method comprises determining an interpolated response profile that best fits the diagnostic profile (i.e., similarity is the greatest between the interpolated response profile and the diagnostic profile). The interpolated response profile comprises measurements of a second plurality of cellular constituents comprising at least a portion of the first plurality of cellular constituents. The interpolated response profile is obtained by interpolating each of the cellular constituents in response profiles of one or more cells of one or more analogous subjects, each of the response profiles comprising measurements of cellular constituents in cells of one of the analogous individuals at one of a plurality of levels of the disease. Measurements of each cellular constituent contained in the provided response profiles are interpolated as a function of the levels of the disease to generate a interpolated response curve so that a value of the measurement of the cellular constituent at any level of the disease can be extracted over the

range of the level of the disease covered by the response profiles from analogous subject(s). An interpolated response profile which comprises measurements of cellular constituents at a particular level of the disease, including at a level not coincident with one of the plurality of levels but within the range, can thus be obtained by extracting the value of each measurement at the level. The level of the interpolated response profile that best fits the diagnostic profile is determined to be the level of the disease in the subject.

Swift teaches a process for testing the association between an allele and a disease. The process involves a comparison of the proportion of test individuals who have the disease and carry the allele from a set of families in which the allele is present and the proportion of test individuals expected to carry the allele if there is no association between the allele and the disease. Swift does not teach interpolating response profiles each of which corresponds to a level of a disease to obtain interpolated response profiles. Nor does Swift teach determining a level of a disease by determining the interpolated profile which has the greatest similarity to a diagnostic profile. The Examiner contends that statistics described in column 9, line 30, through column 14, line 11, disclose interpolation of response profiles. The Examiner also contends that Swift teaches possible levels of diseases as homozygous normal, homozygous abnormal, and heterozygous. The Examiner further contends that Swift teaches the assessment of a 95% confidence level of a disease state. Applicants first respectfully point out that the section at column 9, line 30, through column 14, line 11 cited by the Examiner discloses statistical analysis of a population of individuals. For example, the Examiner's attention is directed to column 10, lines 54-62, of Swift, where it can be seen that in Swift the statistical analysis is applied to the data set R_i ($i = 1, \ldots N$) for N test individuals, where R_i describes if the ith test individual is a heterozygous or not. The analysis is to determine if an individual carrying a particular allele has an elevated level of risk of a disease as compared to an individual who does not carry the allele. Although standard statistical methods, e.g., maximum likelihood, are used, there is no teaching of interpolating response profiles as the method is used in the presently claimed invention. As matter of fact, in Swift, once the type of allele in an individual is determined, e.g., homozygous or heterozygous, the association with the disease is determined based on the risk level obtained from the statistical analysis of the population of test individuals. Even if, arguendo, Swift's homozygous normal, homozygous abnormal, and heterozygous correspond to different "levels" of a disease as contended by the Examiner, nowhere does Swift teach interpolating between such "levels." Applicants also respectfully point out that the 95% confidence level in Swift is a

confidence level of the level of risk of a disease associated with a heterozygous as determined in the statistical analysis of the population of test individuals, rather than the statistical significance of the similarity between a diagnostic profile and an interpolated profile.

Anderson teaches systems and methods of measuring and analyzing diagnostic tests and assays for diagnosis or risk assessment for patients. In Anderson, diagnostic data are measured using an appropriate test or assay, such as an immunoassay. The measured data are then processed employing data reduction and curve fitting algorithms for accurately determining the presence or concentration of the tested substance (see, e.g., Anderson, column 2, lines 55-62). Thus, contrary to the Examiner's contention, in Anderson, curve-fitting is used for processing measured signals to generate data, e.g., to generate parameters to define the obtained image (see also Anderson, column 23, lines 24-42). Anderson also teaches classifying an image based on the generated parameters by comparing the generated parameters to relevant reference data (Anderson, column 28, line 39, through column 30, line 5) or by a neural network approach (Anderson, column 30, line 6, through column 31, line 33). Nowhere does Anderson teach interpolating *response profiles* each of which corresponds to a level of a disease to obtain an *interpolated response profile*. Nor does Anderson teach determining a level of a disease by determining the interpolated profile which has the greatest similarity to a diagnostic profile. With respect to the Examiner's contention that a 95% confidence levels for response profiling is set in Anderson, Applicants respectfully point out that the cited section of Anderson in fact describes the confidence level of a comparison between the fFN test described in Anderson and the fFN ELISA test known in the art (Anderson, column 8, lines 23-33): the Kappa coefficient of 0.68, which was within the 95% confidence interval, indicated that the results obtained using Anderson's fFN test was consistent with results obtained using the known fFN ELISA test. Such a 95% confidence level is not a significance level of the similarity between a diagnostic profile and an interpolated profile.

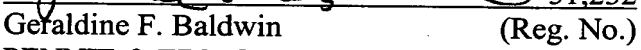
Therefore, Applicants respectfully submit that neither Swift nor Anderson anticipate claims 51-59, and that the rejection under U.S.C. § 102(b) and (e)(2) based on Swift or, in the alternative, the rejection under U.S.C. § 102(e)(2) based on Anderson should be withdrawn.

CONCLUSION

Applicants respectfully request entry of the foregoing amendments and remarks into the file of the above-identified application. Applicants believe that all the pending claims are in condition for allowance. Withdrawal of the Examiner's rejections and allowance of the application are respectfully requested.

Respectfully submitted,

Date: August 4, 2003



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